REMARKS

Status of the Claims

Pending claims

Claims 1 and 2 are pending.

Claims added and amended in the instant amendment

Claims 1 and 2 are amended, and claims 3 to 28 are added. Thus, after entry of the instant amendment, claims 1 to 28 will be pending.

Outstanding Rejections

Claim 2 stands rejected under 35 U.S.C. §112, second paragraph. Claims 1 and 2 stand rejected under 35 U.S.C. §112, first paragraph. Claims 1 and 2 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Gelfand, et al., U.S. Patent No. 5,491,086, issued February 13, 1996, as is evidenced by Bost, et al., (1988) Immunol. Invest. 17:577-586, and Bendayan (1995) J. Histochem. Cytochem. 43:881-886. Claims 1 and 2 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Uemori, et al. (1995) J. Bacteriol. 177:2164-2177, in view of Alisa Campbell, Elsevier Science Publishers, 1984, section 1.1. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to nucleic acids having a sequence with at least about 97%, at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, or at least 50% homology to an exemplary nucleic acid of the invention and fragments comprising at least about 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases thereof, and the sequences complementary thereto, can be found, inter alia, in the paragraph spanning pages 42 and 43, and lines 9 to 15 of page 43. Support for claims directed to polypeptide having a sequence with at least about 97%, at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, or at least 50% homology to an exemplary polypeptide of the invention and fragments comprising at least about 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or

500 consecutive residues, can be found, inter alia, on line 19, page 55 to line 21, page 56. Support for claims directed to antibodies and methods for making and using them can be found, inter alia, on pages 54 to 55.

Information Disclosure Statements

Applicants thank the Examiner for expressly considering (and initialing) the Information Disclosure Statements (IDSs) and Forms PTO-1449, submitted October 2, 2002, and February 4, 2003.

Priority

The specification has been amended to reflect that priority document USSN 09/391,340, has issued as U.S. Patent No. 6,492,511 B2.

Claim objections

The objections to claims 1 and 37 have been addressed in the instant amendment.

Issues under 35 U.S.C. §112, second paragraph

Claim 2 stands rejected under 35 U.S.C. §112, second paragraph, for allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, first paragraph

Enablement

Claims 1 and 2 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention.

The Patent Office states that the specification is enabling for an antibody that specifically binds SEQ ID NO:2 for screening assays (see claims 9, 15 and 27).

However, it is alleged, inter alia, that the specification does not provide reasonable enablement for (i) any purified antibody that specifically binds to any polypeptide having sequences substantially identical to a sequence as set forth in SEQ ID NO:2, or, (ii) any purified antibody that specifically binds to a polypeptide having at least 10 consecutive nucleic

acids of the polypeptides as set forth in SEQ ID NO:2, and sequences substantially identical to a sequence as set forth in SEQ ID NO:2.

Regarding (i), Applicants submit that the instant amendment addresses this issue. After entry of the instant amendment, claim 1 is drawn to antibodies that specifically bind to a polypeptide (a) encoded by a nucleic acid comprising a sequence having at least 70% sequence identity to SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or (b) having polymerase activity and at least 75% sequence identity to a sequence as set forth in SEQ ID NO:2. The term "and sequences substantially identical thereto" has been deleted.

Regarding (ii), Applicants submit that the instant amendment, in part, addresses this issue. After entry of the instant amendment, claim 2 is drawn to antibodies that specifically bind to a polypeptide having at least 30 consecutive amino acids of a polypeptide (a) encoded by a nucleic acid comprising a sequence having at least 70% sequence identity to SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or (b) having at least 80% sequence identity to a sequence as set forth in SEQ ID NO:2. The term "and sequences substantially identical thereto" has been deleted.

The Patent Office also alleged that because the present specification fails to provide sufficient disclosure of amino acid fragments that maintain the structural and functional properties of the exemplary polymerase of the invention, and fails to provide sufficient disclosure of immunogenic fragments, undue experimentation would be required to determine with modifications or fragments would be acceptable to retain activity or immunogenicity.

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of polymerases to practice the claimed invention. As declared by Dr. Jay Short (see attached Rule 132 declaration), the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., screening enzymes, and nucleic acids encoding enzymes, for polymerase activity (e.g., thermostable DNA polymerase activity), was very high. As declared by Dr. Short, using the teaching of the specification, one skilled in the art could have selected routine methods known in the art at the time of the invention to express variants of exemplary enzymes of the invention and screen them polymerase activity. Dr. Short declares that one skilled in the art could have used routine protocols known in the art at the time of the invention, including those

described in the instant specification, to screen for nucleic acids encoding polypeptides having a percent sequence identity to SEQ ID NO:1, or active fragments thereof, for polymerase activity.

Dr. Short also declares that the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art in screening for antibodies that specifically bind to a polypeptide and immunogenic fragments was very high. As declared by Dr. Short, using the teaching of the specification, one skilled in the art could have selected routine methods known in the art at the time of the invention to make antibodies and screen them for specific binding to exemplary enzymes of the invention; and, one skilled in the art could have selected routine methods known in the art at the time of the invention to select and/or screen for immunogenic fragments.

Dr. Short declares that it was routine to screen for multiple substitutions or multiple modifications of an enzyme-encoding sequence and predictably achieve positive results, e.g., making and identifying variant polymerases or immunogenic fragments of polymerases of the invention. As declared by Dr. Short, while the numbers of samples needed to be screened may have been high, the screening procedures were routine and successful results (i.e., finding variant polymerases and immunogenic fragments, and the nucleic acids encoding them) predictable.

Furthermore, Dr. Short declares that it would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with polymerase activity or immunogenicity to create variants or fragments of the exemplary enzymes of the invention and to make and screen them for polymerase activity or immunogenic activity. Accordingly, it would not have taken undue experimentation to make and use the claimed invention, including the genus of polymerases of the invention used to make the antibodies of the invention, and immunogenic fragments of the genus of polymerases of the invention.

Whether large numbers of compositions (e.g., enzymes, antibodies, nucleic acids, and the like) must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. The Federal Circuit in In re Wands directed that the focus of the

enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In Hybritech, Inc., a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of the biological sciences for the instant invention also recognize the need to screen numbers of negatives to find a sample that has the desired properties, e.g., polymerase or immunogenic activity. Furthermore, as declared by Dr. Short, the screening procedures used to identify polymerases and immunogenic fragments within the scope of the instant invention were all well known in the art and at the time this application was filed. All were routine protocols for the skilled artisan. Thus, the skilled artisan using Applicants' written disclosure could practice the instant claimed invention without undue experimentation.

Accordingly, Applicants respectfully submit that the pending claims meet the written description and enablement requirements under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Written Description

Claims 1 and 2 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter not described in the specification in such as way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Patent Office states that the specification was in possession of an antibody that specifically binds SEQ ID NO:2 (see claims 9, 15 and 27).

However, it is alleged, inter alia, that Applicant was not in possession of (i) any purified antibody that specifically binds to any polypeptide having sequences substantially identical to a sequence as set forth in SEQ ID NO:2, or, (ii) any purified antibody that specifically binds to a polypeptide having at least 10 consecutive nucleic acids of the polypeptides as set forth in SEQ ID NO:2, and sequences substantially identical to a sequence as set forth in SEQ ID NO:2.

Regarding (i), Applicants submit that the instant amendment addresses this issue. After entry of the instant amendment, claim 1 is drawn to antibodies that specifically bind to a polypeptide (a) encoded by a nucleic acid comprising a sequence having at least 70% sequence identity to SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or (b) having polymerase activity and at least 75% sequence identity to a sequence as set forth in SEQ ID NO:2. The term "and sequences substantially identical thereto" has been deleted.

Regarding (ii), Applicants submit that the instant amendment, in part, addresses this issue. After entry of the instant amendment, claim 2 is drawn to antibodies that specifically bind to a polypeptide having at least 30 consecutive amino acids of a polypeptide (a) encoded by a nucleic acid comprising a sequence having at least 70% sequence identity to SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or (b) having at least 80% sequence identity to a sequence as set forth in SEQ ID NO:2. The term "and sequences substantially identical thereto" has been deleted.

It is also alleged that because Applicant disclosed only one exemplary amino acid sequence (SEQ ID NO:2), the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims.

Applicants respectfully submit that the claimed invention is sufficiently described

in the specification such that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing. Applicants respectfully aver that a single species of a genus can be sufficient to put one of skill on the art in possession of all species with a claimed genus.

Applicants respectfully submit that only structurally and functionally related enzymes are specifically bound by the antibodies of the invention. Applicants respectfully submit that only structurally and functionally related antibodies are encompassed by the scope of the claims. The enzymes are specifically bound by the antibodies of the claimed invention are described by structure (the exemplary sequence), a physico-chemical property (percent sequence identity) and function (polymerase activity). All enzymes are specifically bound by the antibodies of the claimed invention must have a percent sequence identity to an exemplary polymerase coding sequence. Applicants respectfully submit that describing a genus of polypeptides (and, the antibodies that specifically bind to them) in terms of physico-chemical properties (e.g., sequence identity or hybridization conditions) and function (e.g., encoding polypeptides having polymerase activity) satisfies the written description requirement of section 112, first paragraph.

The Patent Office alleged that a single species of a genus is insufficient to put one of skill on the art in possession of all species within a claimed genus. However, Applicants respectfully aver that even a single species of the instant invention is sufficient to put one of skill on the art in possession of the claimed genus. There is no bright line rule that a single species of a genus is insufficient to put one of skill on the art in possession of all species with a claimed genus. Applicants respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph. In example 14 of the guidelines (a copy of which is attached as Exhibit A), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions. Procedures for making proteins with

substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Analogously, the enzymes specifically bound by the antibodies of the claimed invention is described by structure (the exemplary polypeptide sequences), a physico-chemical property (percent sequence identity) and function (having a polymerase activity). All enzymes specifically bound by the antibodies of the claimed invention must have a percent sequence identity to an exemplary sequence of the invention. The USPTO guidelines recognize that written description is met for a genus of polypeptides described by structure, a physico-chemical property (e.g., a % sequence identity, hybridization under specific conditions) and a defined function (e.g., polymerase activity), the genus of claimed polypeptides also meet the written description requirements of section 112.

The genus of nucleic acids of the claimed invention also fully comply with the requirements for written description of a genus of nucleic acids as set forth in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997). In Lilly, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*" (emphasis added) Lilly, 43USPQ2d at 1406.

As noted above, the instant claims clearly set forth specific structural and physical characteristics of the enzymes specifically bound by the antibodies of the claimed invention. The genus of polypeptides all must have polymerase activity and a specific physical characteristic, e.g., a % sequence identity to an exemplary sequence of the invention. Therefore, the genus of enzymes specifically bound by the antibodies of the claimed invention is defined via shared physical and structural properties in terms that "convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention." (Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991)).

More recently, the Federal Circuit stated

Similarly, in this court's most recent pronouncement, it noted:

> More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the function of the enzymes specifically bound by the antibodies of the claimed invention is sufficiently correlated to a particular, known structure (the exemplary sequences) and a physical (physico-chemical) property (percent sequence identity or specific hybridization conditions). Accordingly, the enzymes specifically bound by the antibodies of the claimed invention are defined via shared physical and structural properties in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Applicants also respectfully refer to recently issued claims directed to genuses of polynucleotides based on sequence identity (and stringent hybridization) to an exemplary nucleic acid, see, e.g., recently issued claims directed to, e.g., 72.5% sequence identity, as in USPN 6,593,514; 75% sequence identity, as in USPN 6,586,215; 80% sequence identity, as in USPN 6,596,926; 85% sequence identity, as in USPN 6,590,141 and USPN 6,586,179; 86% sequence identity, as in USPN 6,583,337; 90% sequence identity (and "stringent hybridization"), as in USPN 6,541,684 (see Exhibit B).

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirement under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §102

Gelfand, et al., U.S. Patent No. 5,491,086

Claims 1 and 2 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Gelfand, et al., U.S. Patent No. 5,491,086, issued February 13, 1996 (hereinafter "Gelfand, et al."), as is evidenced by Bost, et al., (1988) Immunol. Invest. 17:577-586, and Bendayan (1995) J. Histochem. Cytochem. 43:881-886. It is alleged (i) that Gelfand, et al., teaches a nucleic acid 71% identical to the instantly disclosed SEQ ID NO:2, and (ii) that the polymerase of Gelfand, et al., comprises several fragments of at least 10 consecutive residues that are 100% identical to fragments of SEQ ID NO:2.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention.

Regarding (i), Applicants submit that the instant amendment addresses this issue. After entry of the instant amendment, claim 1 is drawn to antibodies that specifically bind to a polypeptide (a) encoded by a nucleic acid comprising a sequence having at least 70% sequence identity to SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or (b) having polymerase activity and at least 75% sequence identity to a sequence as set forth in SEQ ID NO:2. Accordingly, after entry of the instant amendment, Gelfand, et al., is not a single prior source that contains each and every limitation of the invention as set forth in claim 1.

Regarding (ii), Applicants submit that the instant amendment also addresses this issue. After entry of the instant amendment, claim 2 is drawn to antibodies that specifically bind to a polypeptide having at least 30 consecutive amino acids of a polypeptide (a) encoded by a nucleic acid comprising a sequence having at least 70% sequence identity to SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or (b) having at least 80% sequence identity to a sequence as set forth in SEQ ID NO:2. Accordingly, after entry of the instant amendment, Gelfand, et al., is not a single prior source that contains each and every limitation of the invention as set forth in claim 2.

Applicants respectfully aver that because Gelfand, et al., is not a single prior source that contains each and every limitation of the claimed invention, the rejection under section 102(b) can be properly withdrawn.

Regarding the Patent Office's discussion about cross-reacting antibodies (i.e., antibodies that are non-specific and will bind to both polymerases of the claimed invention and other polymerases, e.g., the polymerase taught by Gelfand, et al.), Applicants note that the claimed invention is drawn to antibodies that specifically bind to a polypeptide of the invention, i.e., antibodies that will not bind to non-claimed polymerases, e.g., the polymerase taught by Gelfand, et al. Accordingly, "cross-reacting antibodies" are outside of the scope of the instant claimed invention.

Issues under 35 U.S.C. §103

Uemori, et al., in view of Alisa Campbell

Claims 1 and 2 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Uemori, et al. (1995) J. Bacteriol. 177:2164-2177 (hereinafter "Uemori"), in view of Alisa Campbell, Elsevier Science Publishers, 1984, section 1.1 (hereinafter "Alisa Campbell").

The Patent Office alleged that Uemori, et al., teaches (i) a polypeptide 71% identical to the claimed SEQ ID NO:2 of the invention, and, (ii) the highly conserved sequence VIYGDTD, corresponding to amino acids 574 to 580 of SEQ ID NO:2, and several fragments of at least 10 consecutive amino acids that are 100% identical to fragments of SEQ ID NO:2.

The Patent Office notes that Uemori, et al., is defective in that it does not teach antibodies which specifically bind to sequences of the invention.

Regarding (i), Applicants submit that the instant amendment addresses this issue. As discussed above, after entry of the instant amendment, claim 1 is drawn to antibodies that specifically bind to a polypeptide (a) encoded by a nucleic acid comprising a sequence having at least 70% sequence identity to SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or (b) having polymerase activity and at least 75% sequence identity to a sequence as set forth in SEQ ID NO:2. Accordingly, after entry of the instant amendment, Uemori, et al., is further defective in that, inter alia, it does not teach a polymerase of the invention of claim 1.

Alisa Campbell does not teach a polymerase of the claimed invention. Accordingly, Alisa Campbell does not cure the defects in Uemori, et al., to teach the claimed invention, including the invention of claim 1.

Regarding (ii), Applicants submit that the instant amendment also addresses this issue. After entry of the instant amendment, claim 2 is drawn to antibodies that specifically bind to a polypeptide having at least 30 consecutive amino acids of a polypeptide (a) encoded by a nucleic acid comprising a sequence having at least 70% sequence identity to SEQ ID NO:1 and encoding a polypeptide having polymerase activity, or (b) having at least 75% sequence identity to a sequence as set forth in SEQ ID NO:2. Accordingly, after entry of the instant amendment, Uemori, et al., is further defective in that, inter alia, it does not teach a polymerase of the invention of claim 2.

Alisa Campbell does not teach a polymerase of the claimed invention. Accordingly, Alisa Campbell does not cure the defects in Uemori, et al., to teach the claimed invention, including the invention of claim 2.

Applicants respectfully aver that because Uemori, et al. in combination with Alisa Campbell do not teach a polymerase of the claimed invention, the rejection under section 103(a) can be properly withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, Applicants respectfully aver that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs, 35 U.S.C. §102(b), and 35 U.S.C. §103(a). Applicants respectfully submit that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity to discuss any outstanding issues and to work with the Examiner toward placing the application in condition for allowance.

If any necessary additional such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050. Overcharges can be credited to the same account.

Respectfully submitted,

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